

Expression of Notch Proteins in Pyramidal Neurons *in Vivo*

In their recent study, Zheng *et al.* (1) concluded that Notch1 and Notch2 are not expressed in pyramidal neurons in the postnatal mouse forebrain. This conclusion was based upon an inability to detect expression changes *in vivo* after presumptive deletion using their *CaMKII-Cre* line (2, 3). Unfortunately, the authors provided no direct evidence that they efficiently deleted Notch1 or Notch2 in pyramidal neurons *in vivo*. They infer such deletion because (a) their Cre driver deleted other loci in pyramidal neurons, (b) they detected recombined *Notch1* and *Notch2* alleles in brain tissue by PCR, and (c) Cre-expressing retrovirus could delete both alleles *in vitro*. However, (a) recombination efficiency varies at different loci (4), (b) PCR detection of deleted alleles in tissue is uninformative regarding recombination efficiency and which cell type(s) harbor the deletion, and (c) confirming that these alleles are capable of being recombined (which was already known) does not prove that Notch1 and Notch2 were efficiently deleted *in vivo* using their Cre driver. Even if Zheng *et al.* had deleted Notch1 and Notch2 in neurons *in vivo*, the Northern and Western blots they employed to detect reduced expression would be inadequate if neuronal expression represents a modest fraction of the

total Notch1 and Notch2 expression in the brain. In short, the authors have presented a collection of negative data, which are insufficiently compelling to contradict previous studies (including our own) indicating not only that Notch proteins are expressed in pyramidal neurons but that they serve essential functions in that context (5).

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